

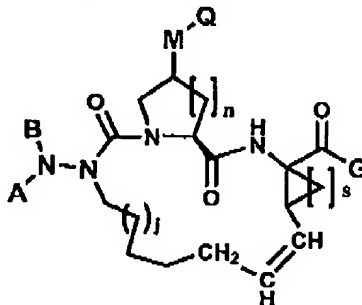
Application No. 10/613,206  
Amendment dated October 24, 2005  
Reply to Office Action of June 22, 2005

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### AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Previously presented) A compound of Formula I:



wherein

A is selected from:

(a) hydrogen;

(b)  $-(C=O)-O-R_1$ , where  $R_1$  is selected from:

1. hydrogen,
2.  $C_1-C_6$  alkyl,
3.  $C_3-C_{12}$  cycloalkyl,
4. substituted  $C_3-C_{12}$  cycloalkyl,
5. aryl,
6. substituted aryl,
7. heteroaryl,
8. substituted heteroaryl,
9. heterocycloalkyl,
10. substituted heterocycloalkyl, or
11.  $-C_1-C_6$  alkyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from

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halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl,  
heterocycloalkyl, or substituted heterocycloalkyl;

(c)  $-(C=O)-R_2$ , where  $R_2$  is selected from:

1.  $-R_1$ , where  $R_1$  is as previously defined,
2. alkylamino,
3. dialkyl amino,
4. arylamino, or
5. diarylamino;

(d)  $-C(=O)-NH-R_2$ , where  $R_2$  is as previously defined;

(e)  $-C(=S)-NH-R_2$ , where  $R_2$  is as previously defined;

(f)  $-S(O)_2-R_2$ , where  $R_2$  is as previously defined;

B is hydrogen or  $C_1-C_6$  alkyl;

G is

- (a)  $-OH$ ;
- (b)  $-O-(C_1-C_{12} \text{ alkyl})$ ;
- (c)  $-NH-R_2$ , where  $R_2$  is as previously defined;
- (d)  $-NHS(O)_2-R_1$ , where  $R_1$  as previously defined;
- (e)  $-(C=O)-R_2$ , where  $R_2$  as previously defined;
- (f)  $-(C=O)-O-R_1$ , where  $R_1$  as previously defined; or
- (g)  $-(C=O)-NH-R_2$ , where  $R_2$  as previously defined;

M is absent or selected from:

- (a)  $-O-$ ;
- (b)  $-S-$ ;
- (c)  $-NH-$ ; or
- (d)  $-NR_1-$ , wherein  $R_1$  is previously defined;

Q is selected from:

- (a) aryl;
- (b) substituted aryl;

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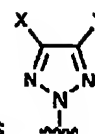
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- (c) heteroaryl;
- (d) substituted heteroaryl;
- (e) heterocycloalkyl; or
- (f) substituted heterocycloalkyl;

j = 0, 1, 2, 3, or 4;

n = 0, 1, or 2; and

s = 0, 1, or 2.



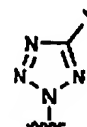
2. (Previously presented) A compound of formula I, wherein M is absent and Q is , wherein X and Y are each independently selected from:

- a)  $-C_1-C_6$  alkyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- b)  $-C_2-C_6$  alkenyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- c)  $-C_2-C_6$  alkynyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- d) aryl;
- e) substituted aryl;
- f) heteroaryl;
- g) substituted heteroaryl;
- h) heterocycloalkyl; or
- i) substituted heterocycloalkyl;

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or in the alternative, X and Y are taken together with the carbons to which they are attached to for a cyclic moiety selected from: aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;



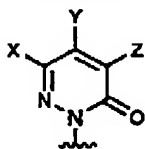
3. (Previously presented) A compound of formula I, wherein M is absent and Q is  wherein Y is selected from:

- a)  $-C_1-C_6$  alkyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- b)  $-C_2-C_6$  alkenyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- c)  $-C_2-C_6$  alkynyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- d) aryl;
- e) substituted aryl;
- f) heteroaryl;
- g) substituted heteroaryl;
- h) heterocycloalkyl; or
- i) substituted heterocycloalkyl;

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4. (Previously presented) A compound of formula I, wherein M is absent and Q is



wherein X, Y, and Z are each independently selected from:

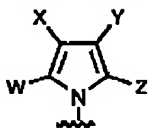
- $-C_1-C_6$  alkyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- $-C_2-C_6$  alkenyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- $-C_2-C_6$  alkynyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- aryl;
- substituted aryl;
- heteroaryl;
- substituted heteroaryl;
- heterocycloalkyl; or
- substituted heterocycloalkyl;

or in the alternative, X and Y or Y and Z are taken together with the carbons to which they are attached to for a cyclic moiety selected from: aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;

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5. (Previously presented) A compound of formula I, wherein M is absent and Q is



wherein W, X, Y, and Z are each independently selected from:

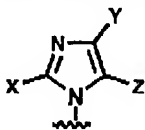
- a)  $-C_1-C_6$  alkyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- b)  $-C_2-C_6$  alkenyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- c)  $-C_2-C_6$  alkynyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- d) aryl;
- e) substituted aryl;
- f) heteroaryl;
- g) substituted heteroaryl;
- h) heterocycloalkyl; or
- i) substituted heterocycloalkyl;

or in the alternative, W and X, X and Y, or Y and Z are taken together with the carbons to which they are attached to for a cyclic moiety selected from: aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;

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6. (Previously presented) A compound of formula I, wherein M is absent and Q is



wherein X, Y, and Z are each independently selected from:

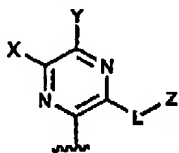
- a)  $-C_1-C_6$  alkyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- b)  $-C_2-C_6$  alkenyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- c)  $-C_2-C_6$  alkynyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- d) aryl;
- e) substituted aryl;
- f) heteroaryl;
- g) substituted heteroaryl;
- h) heterocycloalkyl; or
- i) substituted heterocycloalkyl;

or in the alternative, Y and Z are taken together with the carbons to which they are attached to for a cyclic moiety selected from: aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;

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7. (Previously presented) A compound of formula I, wherein M is -O- and Q is



wherein

L is M, where M is as previously defined;

X, Y, and Z are each independently selected from:

- a)  $-C_1-C_6$  alkyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- b)  $-C_2-C_6$  alkenyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- c)  $-C_2-C_6$  alkynyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- d) aryl;
- e) substituted aryl;
- f) heteroaryl;
- g) substituted heteroaryl;
- h) heterocycloalkyl; or
- i) substituted heterocycloalkyl;

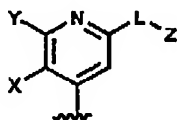
or in the alternative, X and Y are taken together with the carbons to which they are attached to for a cyclic moiety selected from: aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;



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8. (Previously presented) A compound of formula I, wherein M is  $-O-$  and Q is



wherein

L is M, where M is as previously defined;

X, Y, and Z are each independently selected from:

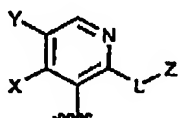
- a)  $-C_1-C_6$  alkyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- b)  $-C_2-C_6$  alkenyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- c)  $-C_2-C_6$  alkynyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- d) aryl;
- e) substituted aryl;
- f) heteroaryl;
- g) substituted heteroaryl;
- h) heterocycloalkyl; or
- i) substituted heterocycloalkyl;

or in the alternative, X and Y are taken together with the carbons to which they are attached to for a cyclic moiety selected from: aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl; or

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9. (Previously presented) A compound of formula I, wherein M is -O- and Q is



wherein

L is M, where M is as previously defined;

X, Y, and Z are each independently selected from:

- a)  $-C_1-C_6$  alkyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- b)  $-C_2-C_6$  alkenyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- c)  $-C_2-C_6$  alkynyl containing 0, 1, 2, or 3 heteroatoms selected from O, S, or N, optionally substituted with one or more substituent selected from halogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl;
- d) aryl;
- e) substituted aryl;
- f) heteroaryl;
- g) substituted heteroaryl;
- h) heterocycloalkyl; or
- i) substituted heterocycloalkyl;

or in the alternative, X and Y are taken together with the carbons to which they are attached to for a cyclic moiety selected from: aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocycloalkyl, or substituted heterocycloalkyl.

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10. (Previously presented) A compound according to claim 1 represented by formula I selected from:

Compound of formula I, wherein A = Boc, B = hydrogen, G = OEt, M = -O-, Q = hydrogen, and j = n = s = 1;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OEt, M = -O-, Q = -S(O)<sub>2</sub>CH<sub>3</sub>, and j = n = s = 1;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OEt, M = -O-, Q = 2-thiophenyl-quinolin-4-yl, and j = n = s = 1;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M = -O-, Q = 2-thiophenyl-quinolin-4-yl, and j = n = s = 1;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OEt, M is absent, Q = 4,5-diphenyltriazol-2-yl, and j = n = s = 1;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M is absent, Q = 4,5-di-thiophenyltriazol-2-yl, and j = n = s = 1;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M is absent, Q = 4-(thiophen-3-yl)-5-(p-methoxyphenyl)triazol-2-yl, and j = n = s = 1;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M is absent, Q = 4-(n-butyl)-5-phenyltriazol-2-yl, and j = n = s = 1;

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Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M is absent, Q = 5-(3-methoxyphenyl)tetrazol-2-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M is absent, Q = 5-(4-pyridyl)tetrazol-2-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M is absent, Q = 5-(3,4-dichlorophenyl)tetrazol-2-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M is absent, Q = 5-(3-bromo-4-methoxy-phenyl)tetrazol-2-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M is absent, Q = 4-(4-fluoro-phenyl)-6-phenyl-1H-pyridazin-3-on-2-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M is absent, Q = 6-phenyl-5-piperidin-1-yl-1H-pyridazin-3-on-2-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M = -O-, Q = 7-Methoxy-2-phenyl-quinolin-4-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M = -O-, Q = 7-Methoxy-2-thiazolyl-quinolin-4-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M = -O-, Q = 7-Methoxy-2-thiophenyl-quinolin-4-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M = -O-, Q = 7-Methoxy-3-(thiophen-2-yl)-1H-quinoxalin-2-yl, and  $j = n = s = 1$ ;

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Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M = -O-, Q = 6-Methoxy-3-(thiophen-2-yl)-1H-quinoxalin-2-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M = -O-, Q = 7-Methoxy-3-[2-(thiophen-2-yl)vinyl]-1H-quinoxalin-2-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M = -O-, Q = 6-Methoxy-3-[2-(thiophen-2-yl)vinyl]-1H-quinoxalin-2-yl, and  $j = n = s = 1$ ;

Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M = -O-, Q = 7-Methoxy-3-[2-(pyridin-2-yl)vinyl]-1H-quinoxalin-2-yl, and  $j = n = s = 1$ ; or

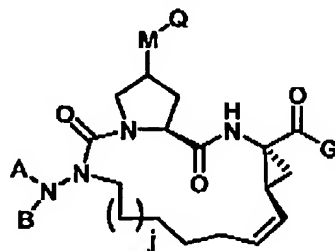
Compound of formula I, wherein A = Boc, B = hydrogen, G = OH, M = -O-, Q = 7-methoxy-3-[2-(pyridin -2-yl)vinyl]-1H-quinoxalin-2-yl, and  $j = n = s = 1$ .

11. (Previously presented) A pharmaceutical composition comprising an anti-hepatitis C virally effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt, ester, or prodrug thereof, in combination with a pharmaceutically acceptable carrier or excipient.
12. (Previously presented) A method of treating a hepatitis C viral infection in a mammal, comprising administering to the mammal an anti-hepatitis C virally effective amount of a pharmaceutical composition according to claim 11.
13. (Previously presented) A method of inhibiting the replication of hepatitis C virus, the method comprising supplying a hepatitis C viral NS3 protease inhibitory amount of the pharmaceutical composition of claim 11.

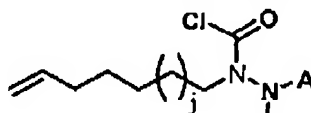
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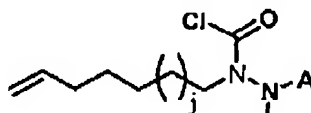
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14. (Previously presented) The method of claim 13 further comprising administering concurrently an additional anti-hepatitis C virus agent.
15. (Previously presented) The method of claim 14, wherein said additional anti-hepatitis C virus agent is selected from the group consisting of:  $\alpha$ -interferon,  $\beta$ -interferon, ribavarin, and adamantine.
16. (Previously presented) The method of claim 14, wherein said additional anti-hepatitis C virus agent is an inhibitor of another target in the hepatitis C virus life cycle, which is selected from the group consisting of: helicase, polymerase, metalloprotease, and IRES.
17. (Previously presented) A process of making compounds of formula I:



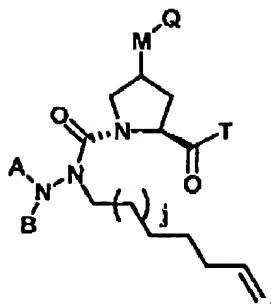
wherein A, B, G, M, Q, j, n, and s are as defined in claim 1, comprising the steps of:



- (a) reacting a compound of formula (A): , wherein A, B, and j is as defined in claim 1 with a hydroxyproline ethyl ester derivative of formula (B): in the presence of a base to form a compound of formula (C):

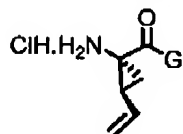
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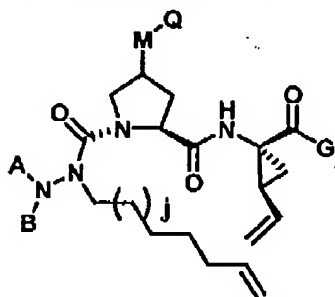


wherein A, B, and j are as defined in claim 1 and T is selected from OH, OMe, or OEt;

(b) reacting a compound of formula B with a compound of formula (D):



, wherein G is as defined in claim 1, under standard amide formation conditions to form a compound of formula (E):



, wherein A, B, G, M, Q, and j are as defined in claim 1;

and

reacting compound of formula E with a Ruthenium-based catalyst.